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WITH COMPLIMENTS OF THE AUTHOR.

CHLORINATED OIL

AND THE

Chlorine Substitution in Fat Oils.

PEPO AS A TÆNIFUGE.

REPRINT OF PAPERS

—BY—

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PHILADELPHIA:

Merrihew Print (J. Spencer Smith), 501 Chestnut St.

1882.

CHLORINATED OIL AND THE CHLORINE SUBSTITUTION IN FAT OILS.

By L. Wolff, M.D.

Read at the Pharmaceutical Meeting, May 16th.

The use of chlorine gas, in the form of chlorine water, in chronic affections of the skin, is by no means of recent origin, and already Thénard and Cluzel recommended the frequent immersion in chlorine water of the hands of those afflicted with itch, by which they claimed to have obtained most excellent and rapid results.

About fifteen years ago I had cause to try it, and had a most excellent success with it; though, to make its effect more lasting and emollient, I experimented with a liniment composed of equal parts of olive oil and chlorine water. The efficacy of this was not less potent, but the absence of any of the chracteristic odor of the gas in this liniment struck me as very peculiar, and I attributed it to a chemical change taking place. As a part of this latter would naturally have to result in the formation of hydrochloric acid, the question arises, if it is the latter or the chlorine gas which had combined with the oil that gave the beneficial results. As the free chlorine in the water, however, had proved effective, the inference is that the chlorine in combination with the oil had given the curative effect.

To test this matter, I was urged by my friend, Dr. J. V. Shoemaker, to make a chlorine compound with oil free from hydrochloric acid, which in the course of therapeutic experiments proved equally effective.

To prepare it I induced a stream of dry chlorine gas, generated in the usual way, into a quantity of oil equal to that of the water in making the chlorine water of the Pharmacopœia, but, to my surprise, found that I was unable to supersaturate the oil, as I had done with the water, no free chlorine becoming at any time evident, until after many days of experiment I ultimately succeeded in my purpose.

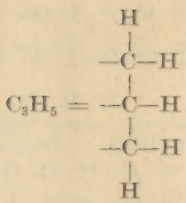
The oil so treated showed at first but little change, save that of turbidity, which could not have been due to water being present, as the gas had been well dried. It soon warmed and heated, and vapors of hydrochloric acid were then evolved. It had changed its color but little, grew viscid and of the specific gravity of 1·059. It is insoluble in alcohol, disproving the presence of free oleic acid; when washed with an equal bulk of water, to free from adherent hydrochloric acid, it showed an emulsifiant tendency. Dissolved therefrom with benzin, and the latter evaporated after previously filtering the solution, it left a product such as I here exhibit. Neutral to test paper at first, it grew acid at standing for some time, with well marked turbidity, thus proving the loosely molecular combination of the chlorine, which, being again substituted by hydroxyl, forms more hydrochloric acid. It possesses no marked odor, and certainly not that of chlorine, and varied in taste but little from that of ordinary oils, no irritant action being manifest when applied to the tissues.

An inquiry on this subject at our former meetings led me to investigate this matter more thoroughly, and I arrived at results which, from a chemical point of view, turned out very interesting.

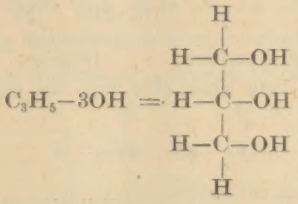
In order to understand the chemistry of this process it is necessary, however, to enter somewhat into the molecular position of the vegetable and animal oils and fats to show exactly where and how a chlorine substitution can take place.

Vegetable and animal oils consist in the main of two principles: one of them, forming on saponification, either with or without great heat or alkalies, is an alcohol named glycerin; the other, forming acids, are termed relatively stearic, palmitic and oleic acids, etc. The radicals of these two constituents are for the former termed propenyl or glyceryl, while for the latter they are known as stearyl, palmityl, and for that which forms the greatest part of the liquid and semi-liquid fats, oleyl.

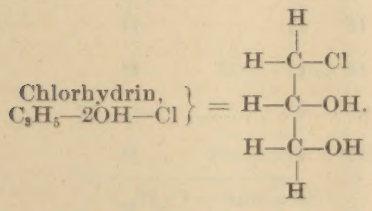
While the propenyl would be expressed as follows:

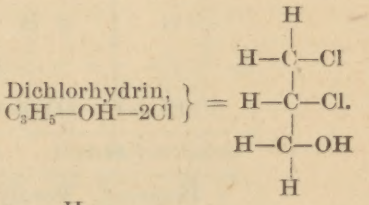


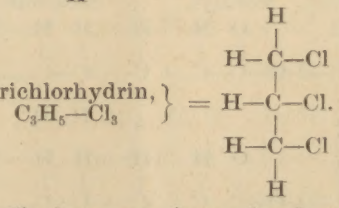
the glycerin or its triatomic alcohol would be constituted thus:



The three molecules of hydroxyl in the glycerin are easily substituted by several elements or compounds, such as acetic, benzoic, hydrochloric, hydrobromic and other acids; to illustrate this I give below the molecular position of mono-, di- and tri-chlorhydrins:





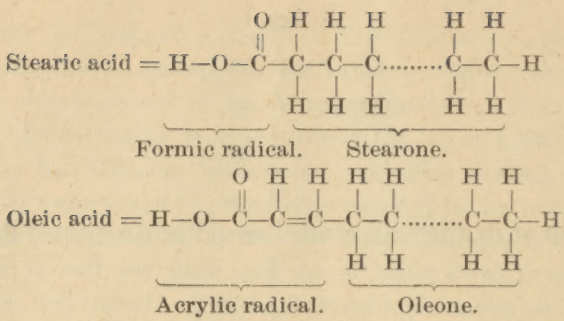


In the fats and oils, however, the molecules of hydroxyl of the glycerin are substituted by the radicals of the fatty acids, such as stearyl, palmityl and oleyl, producing ethers, as which fats and oils must be viewed, as for instance:

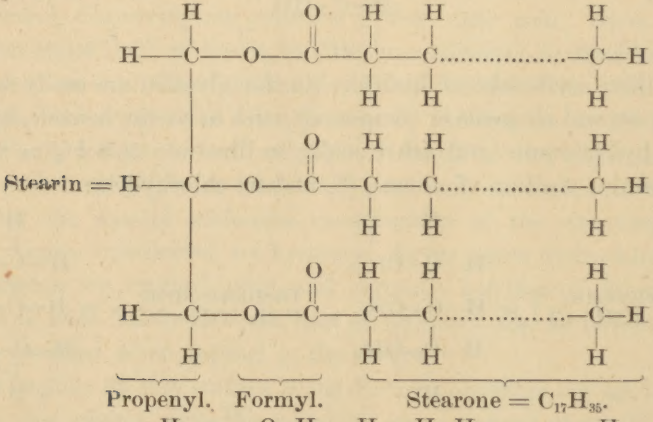
Stearins or Propenyl tristearyls = $C_3H_5.3(C_{18}H_{35}O_3)$

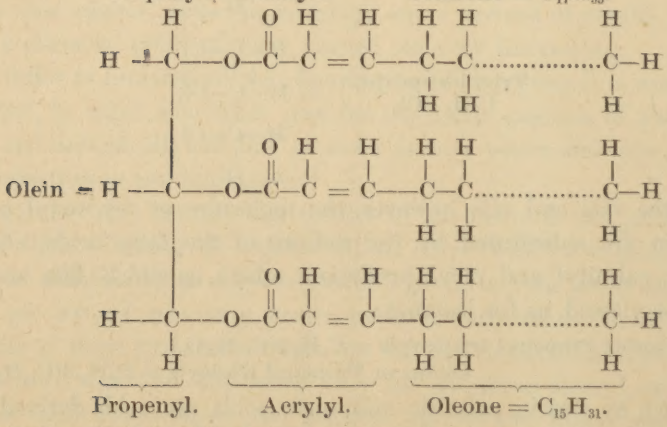
Oleins or Propenyl trioleyls = $C_3H_5.3(C_{18}H_{33}O_2)$

Again, as stearic, palmitic and oleic acids are acids derived from stearyl, palmityl and oleyl, and have an analogous constitution, the former belonging to the series of formic and the latter to that of acrylic acids, their relative constituents must be grouped as follows:



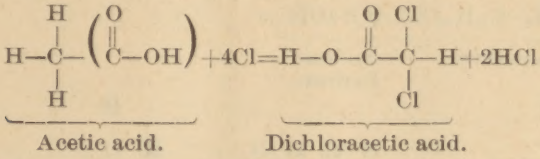
Thus the constitution of fats and oils will be represented by the following diagrams:



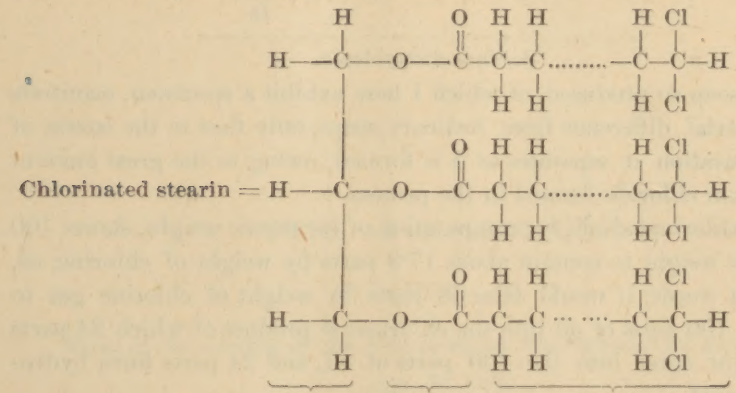


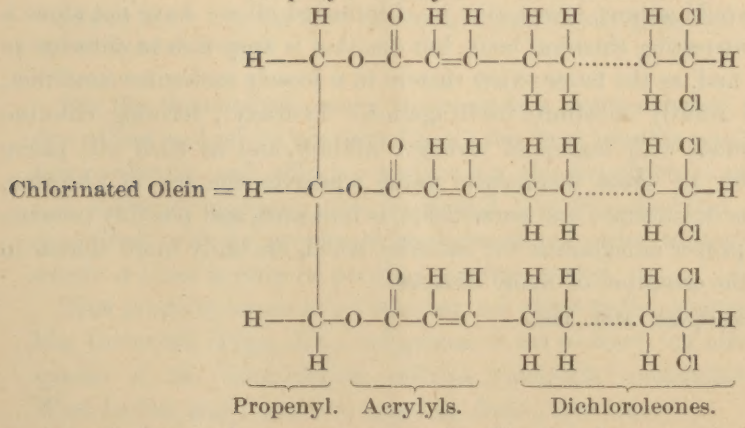
Therefore, if free chlorine gas comes in contact with these molecules, it cannot attack the propenyl, as this is already substituted by the stearyl and oleyl. Again, the stearyl and oleyl cannot be acted on by

the chlorine in their acid nuclei, according to the analogy established by the formation of dichloracetic acid, as will be seen herein:



The chlorine must act, therefore, on the hydrocarbon appendices, $C_{17}H_{35}$ and $C_{15}H_{31}$, substituting therein the relative hydrogens by chlorine, resulting in a molecular position as shown below:

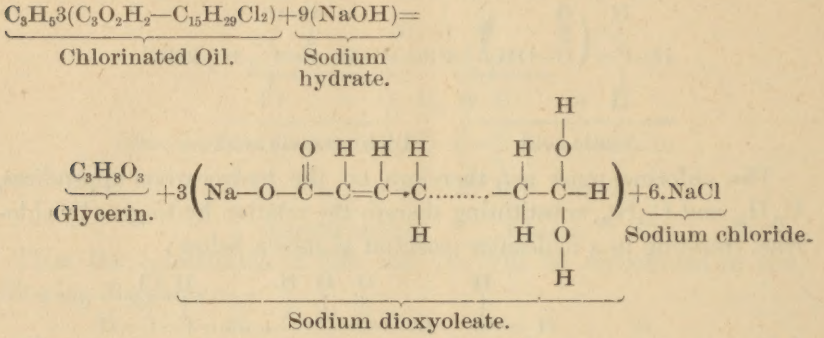




As palmitin and stearin are much alike in their constitution, a reproduction of the structural formula of the former is unnecessary.

As this chlorinated oil is saponifiable with boiling solutions of the hydrates of alkalies, yielding soap, glycerin and chlorides, I would

give below a diagram illustrating its saponification with sodium hydrate:



The soap so produced, of which I here exhibit a specimen, manifests no material difference from ordinary soaps, only that in the course of its preparation it separates as it is formed, owing to the great amount of sodium chloride formed in the process.

The chlorinated oil, by computation of its atomic weight, shows 100 parts by weight to contain about 17·9 parts by weight of chlorine, or, in other words, it would take 48 parts by weight of chlorine gas to convert 100 parts of oil into the chlorinated product of which 24 parts by weight enter into the 100 parts of oil, and 24 parts form hydrochloric acid.

It would appear, hence, that in chlorinated oil we have not alone a very interesting chemical body, but one that is very rich in chlorine as well; and, as the latter exists therein in a loosely molecular condition, it will readily substitute itself again for hydroxyl, forming chlorine compounds with bodies of stronger affinity, and as such will prove probably of great therapeutic value wherever the use of chlorine, both as disinfectant and parasiticide, is indicated, and possibly presenting a proper antagonistic for bacteriæ, which are daily more shown to form the causation of many diseases.

Philadelphia, May, 1882.

PEPO AS A TÆNIFUGE.

By L. Wolff, M. D.

Read at the meeting of the Pennsylvania Pharmaceutical Association, June 14, 1882.

Query No. 7.—What is the best form of administering the seed of Pumpkin (Cucurbita Pepo)?

For the object of this query, to obtain in a pharmaceutical preparation of the seed of "Cucurbita Pepo" the best passible results in the most palatable and effective manner for the expulsion of tapeworm, it is absolutely necessary that we should be well acquainted with the drug itself and its proximate constituents, in order to ascertain to which of these it owes its peculiar tænifuge power.

This property seems to be inherent, not alone to the common pumpkin, Cucurbita Pepo, *Lin.*, indigenous to our country, but also to other species of the cucurbitaceæ, such as Cucurbita occidentalis of the West Indies, and Cucurbita maxima, *Duch.*, and others.

Pepo, though well known for ages as a domestic authelmintic and tænifuge, was brought to the notice of the profession in 1845 by Bruner, who reported twenty-five or thiry successful cases of tænia treated with it. Others have since then used this article largely for the same

purpose, but only with varying success. As the action of any drug cannot be determined without a thorough knowledge of the principle or principles to which it owes its peculiar efficacy, these must be closely studied before a rule can be laid down for its use with a view to its uniform action.

Pepo has been repeatedly examined and investigated by many able authorities, but the results have at all times been conflicting as to the nature of its active ingredients. Its general constituents have been uniformly established as fixed oils, starch, cellulose, pectin and protein compounds, while free fatty acids, sugar, resin and even a glucoside have also been claimed to exist therein. To test this latter I have made an extensive series of experiments in order to be able to either verify or disprove of them. As none of the former ingredients can be viewed as tænifuge in their nature, and this drug itself is such in a marked degree, the inference is that a peculiar principle exists in it to which it owes its remedial property.

Dorner and Wolkowich (1870) claimed to have discovered in pumpkin seed an alkaloid which they proposed to call cucurbitin (cucurbitia?) but which, both as an alkaloid as well as a glucoside, Kapylow (1876) has failed to establish. Sloss attributes its action to the oil, of which he gives a description in the "Pharmaceutische Centralhalle," but advises the use of an electuary of the seed as a tapeworm remedy. Herard thinks its active principle in the kernel and Lelievre in the gemmule. Heckel maintains that it is contained in the menisperm, and to prove it has given this exclusively with good effect. Of the resin extracted from it he gave 75 centigrammes in six pills, expelling the tapeworm. This amount would represent 17 grammes of the green membrane, or 250 grammes of peeled seed.

In further experiments, about six ounces of the perisperm, tegumentum and testæ were given without result, while one ounce of the membrane surrounding the embyro expelled the parasite. This membrane was found to consist of two layers, the outer of which contained a quantity of resin (1 in 17).

As opinions of investigators on this subject are so much divided, and with a view presenting a definite answer to this query, I was led to experiment personally, going over the entire field, in numerous examinations and observations.

While I found my results to correspond with the nature and quality of the general constituents, I am slightly at variance with Sloss and

Kapylow in regard to the oil. While I found it to be a glyceride of oleic, palmitic and myristic acids, I could not detect at any time any free fatty acids in the recently dried seeds, nor could I confirm the fractional solubility of the oil in alcohol, and must attribute their results to the spontaneous decomposition of the oil in old seed into fatty acids and glycerine. While they assert that the expressed oil possessed tænifuge properties, I have not been able to verify this, nor have I observed it in the oil of Pepo which was extracted with petroleum benzin but found it markedly so in oil extracted with ether or chloroform.

My experiments for the separation of an alkaloid or glucoside have also been unsuccessful, and I must side with Kapylow in claiming an absence of either of these. I arrived, therefore, by exclusion to entertain the views of Heckel as to a resin forming the active principle of the seed, and extended my experiments in that direction. I exhausted a quantity of recently dried and comminuted seed with petroleum benzin, previously proven not to extract the active ingredient, and the residue was repeatedly treated with ether, chloroform and alcohol; the product on evaporation of the menstruum was a soft resin of a greenish-brown color, an acrid bitter taste, reminding of the oleoresin of male fern in that respect. Oil which had been extracted with ether or chloroform yielded, on shaking with stronger alcohol, a similar substance. This resin, administered in 15 grain doses, certainly possessed tænifuge properties, and I was thus led to regard it as the active principle of Pepo. It would seem from this that stronger alcohol is the proper menstruum for preparations of this kind. As the resin however as well as the fluid extract, did not prove laxative in my observations and the alcoholic strength of the latter besides would contraindicate in the doses required, its use for children, I examined the emulsion of the seed to determine if, and in what quantities, it contained the resin. I evaporated to this end an emulsion of the seed to dryness, and treated it with stronger alcohol, which after filtration left on evaporation a corresponding quantity of the resin, which had evidently been emulsified in the process.

I would therefore, in answer to the above query, recommend as the most desirable and effective preparation for administering the seed of "Cucurbita Pepo" for adults, first, 15 grains of the above-mentioned resin in pill form; second, one to two fluid ounces of the alcoholic fluid extract in broken doses and largely diluted, both of these taken

fasting in the morning, and to be followed two or three hours afterwards, by a dose of castor oil, or better than either of these for children an emulsion of one ounce of the recently dried and finely comminuted seed and half ounce of granular sugar, with four ounces of water, such as I here exhibit and in which the natural oil acts as a mild laxative. This to be also taken in broken doses following closely on each other, after a fast of six to eight hours.

The electuary formed by pounding the decorticated seed into a pulp with sugar has proved with me not alone unreliable but presented in many cases serious abstacles to deglutition.